REMARKS

Amendments

In the above amendment, claims 1, 2, and 13 are cancelled. Claim 2 is cancelled as being essentially a duplicate of claim 1. Claims 1 and 13 have been replaced by new claims 36 and 37. Claim 14 is amended above to explicitly recite that the agents are administered to the female mammal. In addition, claim 14 is amended to delete the phrase "and an estrogen" to make it explicitly clear that daily administration of both a gestogen and an estrogen throughout the entire period is not a requirement of the claim. New independent claim 38 recites that the period is 28 to 84 days. See, e.g., examples 1-8 at pages 9-10 of the specification. In addition, claim 56 recites that the daily amount of gestogen administered remains the same throughout the period. Here again, see, e.g., examples 1-8.

Claims 39-55 are dependent upon new independent claim 38 and recite further aspects of applicants' invention. See, e.g., examples 1-8 at pages 9-10, page 6, lines 14-18, page 7, lines 1-20, and page 11, line 23- page 12, line 9.

Rejection under 35 USC § 112, second paragraph

In the rejection, it is stated that "comprising" is an inclusive term whereas "consisting essentially of" excludes ingredients that affect the basic and novel characteristics of a composition. Applicants do not disagree. The terms "comprising" and consisting essentially of" are well know claim terms under U.S. practice and have clear meanings pursuant to well settled law. Thus, it is respectfully submitted that these terms are more than sufficiently definite. There is nothing indefinite in a method comprising certain steps while one of those steps is said to consist essentially of certain features.

Applicants' claims 14, 36 and 37 recite that the steroid preparation of the first phase consists essentially of a gestagen in an ovulation-inhibiting dose. Thus, if a prior art reference describes administering, during a similar first phase of a similar period, an ingredient in addition to a gestagen in an ovulation-inhibiting dose, and the presence of that additional ingredient changes the method so that it no longer possess the basic and novel characteristics of the claimed invention, then that prior art does not invalidate the claimed invention. With regards to basic

novel characteristics, these would include, *inter alia*, inducing a gestagenic effect during the first phase without inducing an appreciable estrogenic effect. See, e.g., page 4, lines 16-22 and page 7, lines 24-27.

As for claims 4-7, the rejection asserts that these claims fail to further define claim 14, but does not explain the basis for this assertion. Claims 4 and 5 further define the gestagen recited in claim 14. Claims 6 and 7 further define the modes of administration recited in claim 14. These claims are properly dependent.

In view of the above remarks, withdrawal of the rejection is respectfully traversed.

Rejection under 35 USC § 112, first paragraph

Claim 1-7 and 14-30 are rejected under 35 U.S.C. § 112, first paragraph on grounds of alleged lack of enablement. This rejection is respectfully traversed.

Contrary to the assertion in the rejection, Applicants' disclosure provides more than sufficient guidance to objectively enable one of ordinary skill in the art to make and use the claimed invention. The specification provides examples of gestogens and estrogens for use in the claimed method as well as suitable administration dosages. In addition, in Applicants' examples 1-8 specific method embodiments are described. Based on this information and the information available within the art, one of ordinary skill in the art can practice the claimed invention without undue eperimentation.

In the rejection, it is alleged that the claims are broad and the specification does not include any *in vivo* or *in vitro* test data. However, it is respectfully submitted that the claims are not broad, especially in light of the state of the art, nor is it required that *in vivo* or *in vitro* test data be presented in the specification.

Applicants' claims recite a particular type of administration cycle. There is nothing in the rejection to indicate that within the art Applicants' claims are of a broad nature. Compare, for example, the claims of the cited prior art, e.g., Gast, Konnincx, Hodgen, and Jager. In each of these references, the claims refer both to estrogens and gestogens in general.

Furthermore, the field of oral contraceptives is a well developed field. One of ordinary skill in this relevant art is well aware of procedures used for both *in vivo* or *in vitro* testing of oral contraceptive preparations. See, for example, Hodgen (U.S. 5,898,032) regarding *in vivo* studies using monkeys. Moreover, such examples are not needed to objectively enable one of ordinary

skill in the art. See, for example, the disclosures of Konnicx, Gast and Jager, all of which disclose oral contraceptives using particular dosage regimens but do not present any *in vivo* or *in vitro* tests. By now it is well settled law that one of ordinary skill in the art need not disclose that which is well known in the art. See, e.g, *Hybritech Inc. v. Monoclonal Antibodies, Inc.*, 231 USPQ 81 (Fed. Cir. 1986).

All that is required under the statue is objective enablement. It is not required that applicants' disclosure have in vivo or in vitro test results. See, e.g., *In re Marzocchi et al.*, 169 USPQ 367, 369(CCPA 1971):

> The first paragraph of §112 requires nothing more than objective enablement. How such a teaching is set forth, either by the use of illustrative examples or by broad terminology, is of no importance.

An application disclosure which contains a teaching of the manner and process of making and using an invention in terms which correspond in scope to those used in describing and defining the subject matter sought to be patented must be taken in compliance with the enabling requirement of the first paragraph 35 U.S.C. § 112 unless there is reason to doubt the objective truth of statements contained therein relied on for enabling support. *In re Brana, 51 F.3d 1560,* 34 USPQ2d 1436 (Fed. Cir. 1995). *Fiers v. Revel, 984 F.2d 1164,* 24 USPQ2d 1601 (Fed. Cir. 1993). Furthermore, as stated in *In re Marzocchi*, 169 U.S.P.Q. 367, 369 (CCPA 1971), the PTO must have adequate support for its challenge to the credibility of applicant's statements of utility. See also *In re Bundy*, 209 USPQ 48 (CPA 1981).

Also, it is by now well settled law that the test for enablement is not whether any experimentation is needed but whether or not that experimentation is undue. See, *In re Angstadt*, 190 USPQ 214, 219 (CCPA 1976) in which the art involved (catalysis) was acknowledged to be unpredictable. Even a considerable amount of experimentation, or complex experimentation, is permissible if it is routine. See, e.g., *Ex parte Jackson,* 217 USPQ 804, 807 (POBA 1982) and *In re Wands*, 8 USPQ 2d 1400, 1404 (Fed. Cir. 1988)

In view of the above remarks, it is respectfully submitted that Applicants' disclosure provides more than sufficient guidance to objectively enable one of ordinary skill in the art to make and use the claimed invention with no more than routine experimentation. Withdrawal of

the rejection under 35 U.S.C. §112, first paragraph, is respectfully requested.

Rejection(s) Under 35 USC § 103 in view of Gast and/or Koninckx, and the Rejection Under 35 USC § 103 in view of Jager

In the Office Action claims 1-7 and 13-30 are rejected as being obvious in view of Gast and Koninckx for the reasons set forth in the previous Office Action. To clarify the issues for appeal, applicants respectfully asked the Examiner to indicate whether (1) the claims are being rejected in view of Gast or Koninckx, or (2) the claims are being rejected in view of Gast in combination with the disclosure of Koninckx. It appears from the comments in the rejection that these two references are being applied in the alternative. In any event, the rejection is again respectfully traversed.

In addition, claims 1-7 and 13-30 are rejected as being obvious in view of Jager. This rejection is also respectfully traversed.

Gast discloses a method of achieving contraception through the use of a so-called bridged triphasic progestin/estrogen combination regimen. The regimen actually has four phases, the fourth phase is called the estrogen phase and involves administering an estrogen alone. The estrogen alone phase is used to maintain good cycle control. See, e.g., column 5, line 65-column 6, line 14.

In the first phase, which is 3-8 days, the progestin is administered in an amount equivalent to 40-125 μg of levonogestrel and the estrogen is administered in an amount equivalent to 10-20 μg of ethinyl estradiol. In the second phase, which is 4-15 days, the progestin is administered in an amount equivalent to 40-125 μg of levonogestrel and the estrogen is administered in an amount equivalent to 10-20 μg of ethinyl estradiol. In the third phase, which is also 10-15 days, the progestin is administered in an amount equivalent to 40-125 μg of levonogestrel and the estrogen is administered in an amount equivalent to 10-20 μg of ethinyl estradiol. These three phases together last 23-25 days. The estrogen phase follows and lasts 3-5 days during which an estrogen, without progestin, is administered in an amount equivalent to 10-20 μg of ethinyl estradiol. See column 6, lines 15-44.

The levels of progestin and estrogen can vary during the first three phases. For example, the amount of estrogen can stay the same throughout all three phases while the progestin level is higher in the second phase than in the first phase, and higher in the third phase than in the second

phase. On the other hand, for example, the progestin amount can peak during the second phase while the estrogen amount increases from the first phase to the second phase, and from the second phase to the third phase. See the regimens describes in the tables at column 6-7, 8 and 9.

Thus, Gast does not describe or suggest a period of administration in which the initial portion of the period is progestin administration and the reminder of the period is a progestin/estrogen administration. Furthermore, Gast does not describe or suggest a period of administration in which the last part of the period involves administering progestin and estrogen. In fact, this would be contrary to the teaching of Gast which uses an estrogen alone phase at the end of the administration period "to assist in maintaining good cycle control." See column 6, lines 9-14. Modifying the regimen of Gast to administer both an estrogen and a progestin in the final phase of the period would result in a treatment period that administers both an estrogen and a progestin throughout the entire period. There is nothing within the disclosure of Gast that would suggest using an estrogen/progestin combination in the last portion of the period.

Koninckx describes a preparation for substitution therapy and oral contraception. The preparation contains at least one progestogen **and** at least one estrogen, i.e., both an estrogen and a progestogen are administered. See column 2, lines 10-14. In the course of the treatment, the estrogen is administered with periodicity, with the periods being of generally less than 10 days. In addition, it is also possible to administer the progestogen with periodicity.

See, e.g., Examples 1-5 in which alternating periods of 7, 4-5, 4-7, 6 days, and 4 days, respectively, are used. In these examples, a first period of estrogen/progestogen administration is followed by a second phase of estrogen/progestogen administration wherein in the second phase the level of estrogen is higher than in the first phase while the level of progestogen remains the same. In Examples 6 and 7, the levels of estrogen and progestogen are both higher in the second phase than in the first phase (alternating periods of 6 days and 7 days, respectively). Koninckx disclosed these regimens were able to induce amenorrhoea (the absence of menstruation). See, e.g., column 2, lines 5-9 and 32-25. Thus, unlike Gast, Koninckx is directed to eliminating menses rather then maintaining good cycle control. Compare also, for example, applicants' claim 14 and page 5, lines 22-25 of Applicants' specification.

Thus, the regimen of Koninckx involves administering **both** an estrogen and a progestogen on a daily basis throughout the entire period of administration while periodically changing the amount of at least the estrogen in order to induce amenorrhoea. Koninckx does not

provide any suggestion of modifying the regimen in such a manner that would lead to menses. Thus, there is no suggestion of an administration period in which the last phase consists essentially an estrogen. Similarly, there is no suggestion of regimen which has any phase in which a progestogen is administered without an estrogen.

Jager discloses a multi-phase regimen having at least two phases. The first phase consists of 20-22 days during which both an estrogen and a progestogen are administered daily. The second phase consists of 2-10 days during which only a progestogen is administered. Both the first phase and the second phases can contain subphases. See, e.g., page 4, lines 1-22. It is during the final phase, when the administered active ingredients change from both estrogen and progestogen to just progestogen, that withdrawal bleeding occurs. Clearly, Jager provides no suggestion of administering an estrogen during the final phase of a treatment period, let alone the combination of an estrogen and a progestogen.

Applicants do not dispute that Gast, Koninckx, and Jager disclose contraceptive methods which employ gestagens and estrogens. However, none of the references, taken together or separately, or knowledge available to one of skill in the art, discloses or suggests the particular manner in which these agents are combined, or the schedule of their administration, as recited in the instant claims.

As is well known in the art, the levels of various hormones in female mammals vary during the menstrual cycle. Thus, for example, the levels of estrogen and progestogen, as well as other hormones, will vary cyclically in conjunction with the menstrual cycle. As a result, it is well known in the art of methods of hormonal therapy, especially contraception, that the dosage regimen, *i.e.*, the sequence and duration of administration of particular combinations of hormonal agents, is an important factor with regard to, *e.g.*, efficacy, potential side effects, patient compliance, and the like. Moreover, many of the disclosures within the art are devoted to using different dosage regimens. Thus, the art doesn't recognize one particular dosage regime as being the optimal one.

Furthermore, the very fact that two of the cited references are U.S. *patents* which claim contraceptive methods utilizing hormones (a gestagen and an estrogen) administered in different combinations and by different schedules, demonstrates the art's recognition that dosage regimen is not a more obvious choice, but instead is used to help distinguish different methods of hormonal therapy and help establish their individual patentability.

The references cited in the rejections, Gast , Konickx, and Jager et al., do not disclose a contraceptive method which suggests administering gestagens and estrogens in accordance with the particular schedules recited in the instant claims. Nor do these references give any suggestion that would lead one of ordinary skill in the art to select combinations and dosage schedules recited in Applicants' claims. The conclusion that the claimed dosage regimens would be obvious without any demonstration within the art that these regimens are suggested is contrary to the art's overall teaching concerning the use of different dosage regimes.

The rejections fails to properly take into consideration the specific combinations and dosage schedules recited in the instant claims. It is improper to simply dismiss features recited in the claims; claimed features cannot be ignored.

> We note at the outset that the claim limitation "to form *** hydroperoxides" must be given effect since we *must* give effect to *all* claim limitations. See In re Geerdes, 491 F.2d 1260, 180 USPQ 789 (CCPA 1974); In re Wilder, 57 CCPA 1314, 419 F.2d 447, 166 USPQ 545 (1970).

In re Angstadt et al., 190 USPQ 214, 217 (CCPA 1976).

This is particularly true for factors regarding dosage regimens in methods of contraception, for the reasons discussed above.

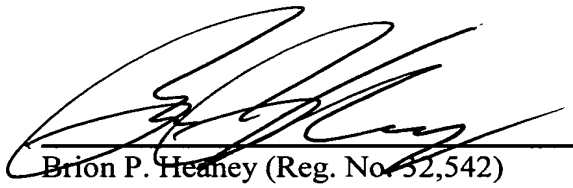
None of the references of record provides sufficient motivation to lead one of ordinary skill in the art to modify any of the methods of the cited references to achieve a method having a dosage regimen (combination and dosage schedule) in accordance with the claimed invention. An assertion of obviousness is determined from the vantage point of a hypothetical person having ordinary skill in the art to which the patent pertains. To assess this determination, the hypothetical person has the relevant prior art references in from of him, but has **no knowledge of applicants' invention**. Motivation is not established simply assumed by piecing together disclosures in the prior art. It is more than this. Motivation describes the rationale as to why one would be directed toward making particular modifications. The more ability to combine parts of the prior art, by hindsight analysis, is not sufficient to establish motivation.

> ... As this court has stated, 'virtually all [inventions] are combinations of old elements ... Therefore, an examiner may often find every element of a claimed invention in the prior art. If identification of each claimed element in the prior art were sufficient to negate patentability, very few patents would ever issue. Furthermore, rejecting patents solely by finding prior art corollaries for the claimed elements would permit an examiner to use the claimed invention itself as a blueprint for piecing together elements in the prior art to defeat the patentability of the claimed invention. Such an approach would be an illogical and inappropriate process by which to determine patentability.
> *In re Rouffet*, 47 USPQ2d 1453, 1457 (Fed. Cir. 1998)

For the reasons discussed above, withdrawal of the prior art rejections and allowance of the application are respectfully requested.

As a final note, the Office Action lists Hodgen (US 5,898,032) on the form PTO-892, but does not apply Hodgen in a rejection. In any event, Hodgen does not disclose or suggest applicants' claimed invention.

Respectfully submitted,



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VERSION WITH MARKINGS TO SHOW CHANGES MADE

14. (Amended) A method of contraception in a female mammal, comprising administering to said mammal a gestagen ~~and an estrogen~~ over a period of at least 28 days, wherein said period has a first phase and a second phase,

wherein said first phase consists essentially of administering an ovulation-inhibiting amount of a gestagen, and said second phase comprises administering an ovulation-inhibiting amount of a gestagen and a natural estrogen in an amount effective to achieve regular menstrual-like bleeding,

wherein said second phase is the last 5 to 10 days of said period and said first phase is the remainder of said period.